

Appl. No. 10/722,820  
Amdt. dated October 17, 2005  
Amendment under 37 CFR 1.116 Expedited Procedure  
Examining Group 1614.

PATENT

This listing of claims will replace all prior versions of claims in the application. Applicants believe that the listing reflects the claims as currently pending in the application. No new amendments are introduced in this paper.

Listing of Claims:

1. (previously presented) A pharmaceutical composition for reducing oxidative damage or delaying senescence comprising an orally administrable effective unit dosage of a primary N-hydroxylamine or a pharmaceutically acceptable salt thereof and substantially free of a nitrone corresponding to the hydroxylamine, wherein the hydroxylamine has the general formula,



wherein  $\text{R}_1$ ,  $\text{R}_2$  and  $\text{R}_3$  are independently selected from: hydrogen, substituted or unsubstituted (C1-C18) alkyl, alkenyl, alkynyl, aryl, oxyl, acyl, carboxyl, amino, nitro, nitroso, oxime, hydrazone, azo, thiol, sulfonyl and halide.

2. (original) A composition according to claim 1, wherein the dosage is from 100 ug to 1g.

3. (previously presented) A composition according to claim 1, wherein at least one of  $\text{R}_1$ ,  $\text{R}_2$  and  $\text{R}_3$  is selected from unsubstituted (C1-C18) alkyl, alkenyl and alkynyl.

4. (previously presented) A composition according to claim 1, wherein at least one of  $\text{R}_1$ ,  $\text{R}_2$  and  $\text{R}_3$  is selected from unsubstituted (C1-C18) alkyl, cycloalkyl, alkenyl and alkynyl, and said at least one of  $\text{R}_1$ ,  $\text{R}_2$  and  $\text{R}_3$  is selected from:  $\text{CH}_3\text{-(CH}_2\text{)}_{n1}$ ,  $\text{(CH}_3\text{-(CH}_2\text{)}_{n2}\text{)}_2\text{CH}$ ,  $\text{(CH}_3\text{-(CH}_2\text{)}_{n2}\text{)}_3$ , cyclopentyl, cyclohexyl,  $\text{(CH}_2\text{=CH-CH}_2\text{)}_{n3}$  and  $\text{(CH=C-CH}_2\text{)}_{n3}$ , wherein  $n1 = 1$  to 18,  $n2 = 1$  to 17 and  $n3 = 1$  to 3.

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5. (previously presented) A composition according to claim 1, wherein the hydroxylamine is selected from:

N-methylhydroxylamine,	N-(n-decahexyl)hydroxylamine,
N-ethylhydroxylamine,	N-(n-decaoctyl)hydroxylamine,
N-n-propylhydroxylamine,	N-isopropylhydroxylamine,
N-(n-butyl) hydroxylamine,	N-sec-butylhydroxylamine,
N-(n-pentyl)hydroxylamine,	N-tert-butylhydroxylamine,
N-(n-hexyl)hydroxylamine,	N-cyclohexylhydroxylamine,
N-(n-heptyl)hydroxylamine,	N-cyclopentylhydroxylamine,
N-(n-octyl)hydroxylamine,	N-(2-propene)hydroxylamine,
N-(n-nonyl)hydroxylamine,	N-(3-butene)hydroxylamine,
N-(n-decyl)hydroxylamine,	N-(2-propyne)hydroxylamine and
N-(n-dodecyl)hydroxylamine,	N-(3-butyne)hydroxylamine.

6. (previously presented) A composition according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted aryl.

7. (previously presented) A composition according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted aryl, and said at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is selected from: mono, di, or tri methyl, methoxy, halo, nitro, amino, hydroxyl and substituted or unsubstituted phenyl, naphthyl, anthryl, phenanthryl, pyridyl, quinoliny, imidazolyl, benzoxazolyl, pyrrolyl, furanyl, piperidinolyl and tetrahydrofuranyl.

8. (previously presented) A composition according to claim 1, wherein the hydroxylamine is selected from:

N-benzylhydroxylamine,	N-(1,3-diaminobenzyl)hydroxylamine,
N-(n-nitrobenzyl)hydroxylamine,	N-(1,3-hydroxybenzyl)hydroxylamine,

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N-(n-methylbenzyl)hydroxylamine,	N-(2,4-diaminobenzyl)hydroxylamine,
N-(n-chlorobenzyl)hydroxylamine,	N-(2,4-dihydroxybenzyl)hydroxylamine,
N-(n-aminobenzyl)hydroxylamine,	Imidazole-2-methylhydroxylamine and
N-(n-hydroxybenzyl)hydroxylamine,	Benzoxazole-2-methylhydroxylamine,

wherein n is selected from 1, 2, 3, 4, 5 and 6.

9. (previously presented) A composition according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted (C1-C18) oxyl.

10. (previously presented) A composition according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted (C1-C18) oxyl and said at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is selected from: hydroxyl, hydroxyalkyl (HO-(CH<sub>2</sub>)<sub>n1</sub>), hydroxyaryl selected from benzylalcohol, phenol and naphthol, alkoxy (O-(CH<sub>2</sub>)<sub>n1</sub>) and aryloxy selected from phenoxy, benzyloxy and naphthyloxy, wherein n1= 1 to 18.

11. (previously presented) A composition according to claim 1, wherein the hydroxylamine is selected from:

N-(hydroxymethyl)hydroxylamine,	N-(methoxymethyl)hydroxylamine,
N-(2-hydroxyethyl)hydroxylamine,	N-(methoxyethyl)hydroxylamine,
N-(3-hydroxypropyl)hydroxylamine,	N-(methoxyisopropyl)hydroxylamine,
N-(4-hydroxybutyl)hydroxylamine,	N-(benzyloxymethyl)hydroxylamine and
N-(6-hydroxyhexyl)hydroxylamine,	N-(4-hydroxymethylbenzyl)hydroxylamine.
N-(12-hydroxydodecyl)hydroxylamine,	

12. (previously presented) A composition according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted (C1-C18) alkylcarboxyl or arylcarboxyl.

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13. (previously presented) A composition according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted (C1-C18) alkyl or aryl carboxyl and said at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is selected from carboxyalkyls and benzyl.

14. (previously presented) A composition according to claim 1, wherein the hydroxylamine is selected from:

N-(carboxymethyl)hydroxylamine,	N-(5-carboxypentyl) hydroxylamine,
N-(2-carboxyethyl)hydroxylamine,	N-(6-carboxyhexyl)hydroxylamine,
N-(3-carboxypropyl)hydroxylamine,	N-(4-carboxybenzyl)hydroxylamine and
N-(4-carboxybutyl)hydroxylamine,	N-(12-carboxydodecyl)hydroxylamine.

15. (previously presented) A composition according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted (C1-C18) ester.

16. (previously presented) A composition according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted (C1-C18) ester and said at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is selected from alkyl (C1 – C18) and aryl esters.

17. (previously presented) A composition according to claim 1, wherein the hydroxylamine is selected from:

N-(acetyloxymethyl)hydroxylamine,  
N-(acetyloxyethyl)hydroxylamine,  
N-(acetyloxypropyl)hydroxylamine,  
N-(propylcarbonyloxy)methylhydroxylamine,  
N-(butylcarbonyloxy)methylhydroxylamine,  
N-(tert-butylcarbonyloxy)methylhydroxylamine,  
N-(benzyloxycarbonyl)methylhydroxylamine,  
N-(phenyloxycarbonyl)methylhydroxylamine,

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N-(3-pyridyloxycarbonyl)methylhydroxylamine and  
N-(benzoxazol-5-carbonyloxy)methylhydroxylamine.

18. (previously presented) A composition according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted (C1-C18) carbonyl.
19. (previously presented) A composition according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted carbonyl and said at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is selected from alkyl (C1 – C18) carbonyls and aryl carbonyls.
20. (previously presented) A composition according to claim 1, wherein the hydroxylamine is selected from:
- |                                       |  |
|---------------------------------------|--|
| N-(acetyl)methylhydroxylamine,        | N-(phenylcarbonyl)methylhydroxylamine  |
| N-(ethylcarbonyl)methylhydroxylamine, | and                                    |
| N-(butylcarbonyl)methylhydroxylamine, | N-(benzylcarbonyl)methylhydroxylamine. |
21. (previously presented) A composition according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted alkyl(C1-C18) or aryl amino.
22. (previously presented) A composition according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted alkyl (C1-C18) or aryl amino and said at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is selected from primary alkyl amine selected from methylamine, ethylamine, propylamine, butylamine and hexylamine, secondary amine selected from dimethylamine, diethylamine and dipropylamine, tertiary amine selected from trimethyl and triethylamine, and quarternary amine selected from tetramethyl and tetra-ethylammonium salts.
23. (previously presented) A composition according to claim 1, wherein the hydroxylamine is selected from:

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N-aminomethylhydroxylamine,  
N-(2-aminoethyl)hydroxylamine,  
N-(N-methylamino)methylhydroxylamine,  
N-(N,N-dimethylamino)methylhydroxylamine,  
N-(N,N,N-trimethylammonium)methylhydroxylamine,  
N-(3-aminopropyl)hydroxylamine,  
N-(6-aminoethyl)hydroxylamine,  
N-(4-aminobenzyl)hydroxylamine,  
Hydroxylamine-1-methylpyridinium and  
Hydroxylamine-1-methylquinolinium.

24. (previously presented) A composition according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted (C1-C18) alkyl or aryl nitro.

25. (previously presented) A composition according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted alkyl(C1-C18) or aryl nitro and said at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is selected from alkyl nitro selected from nitromethyl, nitroethyl, nitropropyl, nitrobutyl, nitropentyl, nitrohexyl and nitrobenzyl, and aryl nitro selected from nitrophenyl and nitronaphthyl.

26. (previously presented) A composition according to claim 1, wherein the hydroxylamine is selected from:

N-(nitromethyl)hydroxylamine,	N-(5-nitropentyl)hydroxylamine,
N-(2-nitroethyl)hydroxylamine,	N-(6-nitrohexyl)hydroxylamine,
N-(3-nitropropyl)hydroxylamine,	N-(4-nitrobenzyl)hydroxylamine and
N-(4-nitrobutyl)hydroxylamine,	N-(2,4-dinitrobenzyl)hydroxylamine.

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27. (previously presented) A composition according to claim 1, wherein at least one of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted (C1-C18) nitroso.
28. (previously presented) A composition according to claim 1, wherein at least one of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted (C1-C18) nitroso and said at least one of  $R_1$ ,  $R_2$  and  $R_3$  is selected from aliphatic nitrosoamines and aromatic nitroso.
29. (previously presented) A composition according to claim 1, wherein the hydroxylamine is selected from:  
N-(N-methyl-N-nitroso-amino)methyl hydroxylamine,  
N-(N-methyl-N-nitroso-2-amino)ethylhydroxylamine,  
N-(N-methyl-N-nitroso-3-amino)propylhydroxylamine and  
N-(p-nitroso)benzylhydroxylamine.
30. (previously presented) A composition according to claim 1, wherein at least one of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted oxime.
31. (previously presented) A composition according to claim 1, wherein at least one of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted (C1-C18) oxime and said at least one of  $R_1$ ,  $R_2$  and  $R_3$  is selected from: acetaldoxime, propionaldoxime, butanaldoxime and benzaldoxime.
32. (previously presented) A composition according to claim 1, wherein the hydroxylamine is selected from:  
Acetaldoxime-3-hydroxylamine, Butanaldoxime-5-hydroxylamine and  
Propionaldoxime-4-hydroxylamine, (4-benzaldoxime)1-methylhydroxylamine.
33. (previously presented) A composition according to claim 1, wherein at least one of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted (C1-C18) hydrazone.

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34. (previously presented) A composition according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted (C1-C18) hydrazone and said at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is selected from: acetaldehyde hydrazone, propanaldehyde hydrozone, butanaldehyde hydrazone and phenylhydrazone.
35. (previously presented) A composition according to claim 1, wherein the hydroxylamine is selected from
- |   |   |
|---|---|
| 1-hydroxylamine-acetaldehyde hydrazone, | 1-hydroxylamine-butanaldehyde hydrazone |
| 1-hydroxylamine-propanaldehyde          | and                                     |
| hydrazone,                              | 1-hydroxylamine-benzylaldehyde          |
|   | hydrazone.                              |
36. (previously presented) A composition according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted azo.
37. (previously presented) A composition according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted azo and said at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is selected from: azobenzene, p-(phenylazo)benzyl and p-diazobenzyl.
38. (previously presented) A composition according to claim 1, wherein the hydroxylamine is selected from:
- N-(p-phenylazo)benzylhydroxylamine,  
N-(p-diazobenzyl)hydroxylamine and  
N-(p-methoxyphenylazo)benzylhydroxylamine.
39. (previously presented) A composition according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted (C1-C18) thiol.



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40. (previously presented) A composition according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted (C1-C18) thiol and said at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is selected from (C1-C18) alkylthiol selected from methyl, ethyl, propyl, butyl, pentyl and hexyl thiol, and arylthiol selected from thiophenol and benzylthiol.

41. (previously presented) A composition according to claim 1, wherein the hydroxylamine is selected from:

N-(thiomethyl)hydroxylamine,	N-(3-thiopropyl)hydroxylamine and
N-(2-thioethyl)hydroxylamine,	N-(p-sulfhydryl)benzylhydroxylamine.

42. (previously presented) A composition according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted (C1-C18) sulfonic acid.

43. (previously presented) A composition according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is substituted or unsubstituted (C1-C18) sulfonic acid and said at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is selected from methanesulfonic acid, ethanesulfonic acid, propanesulfonic acid, butanesulfonic acid and p-toluenesulfonic acid.

44. (previously presented) A composition according to claim 1, wherein the hydroxylamine is selected from:

1-hydroxylamine-methanesulfonic acid,	1-hydroxylamine-butane-4-sulfonic acid
1-hydroxylamine-ethane-2-sulfonic acid,	and
1-hydroxylamine-propane-3-sulfonic acid,	N-(p-sulfobenzyl)hydroxylamine.

45. (previously presented) A composition according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is halide.

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46. (previously presented) A composition according to claim 1, wherein at least one of  $R_1$ ,  $R_2$  and  $R_3$  is halide and said at least one of  $R_1$ ,  $R_2$  and  $R_3$  is selected from F, Cl, Br and I.

47. (previously presented) A composition according to claim 1, wherein the hydroxylamine is selected from:

N-(chloromethyl)hydroxylamine,	N-(4-chlorobutyl)hydroxylamine,
N-(bromomethyl)hydroxylamine,	N-(p-chlorobenzyl)hydroxylamine,
N-(2-chloroethyl)hydroxylamine,	N-(p-fluorobenzyl)hydroxylamine and
N-(3-chloropropyl)hydroxylamine,	N-(p-iodobenzyl)hydroxylamine.

48. (previously presented) A composition according to claim 1, wherein at least one of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted hydroxylamine.

49. (previously presented) A composition according to claim 1, wherein at least one of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted hydroxylamine and said at least one of  $R_1$ ,  $R_2$  and  $R_3$  is selected from N-methylhydroxylamine, N-ethylhydroxylamine, N-propylhydroxylamine N-butylhydroxylamine, N-pentylhydroxylamine, and N-benzylhydroxylamine.

50. (previously presented) A composition according to claim 1, wherein the hydroxylamine is selected from:

Bis-methylhydroxylamine,	Bis-(3-propyl)hydroxylamine and
Bis-(2-ethyl)hydroxylamine,	Bis-benzylhydroxylamine.

51. (previously presented) A composition according to claim 1, wherein at least one of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted (C1-C18) phosphoester.

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52. (previously presented) A composition according to claim 1, wherein at least one of  $R_1$ ,  $R_2$  and  $R_3$  is substituted or unsubstituted (C1-C18) phosphoester and said at least one of  $R_1$ ,  $R_2$  and  $R_3$  is selected from: dimethylphosphate, diethylphosphate, dipropylphosphate and benzylphosphate.

53. (previously presented) A composition according to claim 1, wherein the hydroxylamine is selected from:

di-hydroxylaminemethylphosphate ester,  
mono-hydroxylaminemethylphosphate ester,  
mono-(1-hydroxylamine)-ethyl-2-phosphate ester,  
di-(1-hydroxylamine)-2-ethylphosphate ester,  
di-(1-hydroxylamine)-3-propyl-phosphate ester,  
mono-(hydroxylamine-benzyl-phosphate ester and  
di-hydroxylamine-benzylphosphateester.

54. (original) A composition according to claim 1, wherein the nitro compound is less than 1% (wt/wt) of the hydroxylamine in the composition.

55. (original) A composition according to claim 1 further comprising an effective amount of a carnitine.

56. (original) A method for reducing oxidative damage to, or delaying senescence of a cell comprising the step of contacting a cell subject to or at risk of undesirable oxidative damage or senescence with a composition according to claim 1.

57. (original) A method for reducing oxidative damage to, or delaying senescence of a cell comprising the steps of:

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identifying a cell as subject to or at risk of undesirable oxidative damage or senescence;  
and  
contacting the cell with a composition according to claim 1.

58. (original) A method according to claim 57, wherein the cell is contained in other than a cancerous host.